

REMARKS

Claims 1, 3-8, 25-30, and 33-43 are now pending in the application; claims 6, 7, 25, 26, 35, 36, 38, and 39 are pending but withdrawn. Claims 2, 9-24, 31, 32, and 44 have been canceled. Claims 1, 3, 4, 28, 29, 33, 34, 41 and 42 have been amended. The amendments are supported by the specification. Claim 1 has been amended to recite “the amino terminal ATP binding domain of a heat shock protein 70 (hsp70) or the carboxyl terminal peptide binding domain of an hsp70.” This amendment is supported by the specification at, for example, page 7, line 33 (where Applicant teaches that the hsp can be hsp70), page 17, lines 22-23 (where Applicant teaches that hsp70 and ova-hsp70 were purified), and page 28, lines 13-20 (where Applicant teaches purification of fusion proteins containing ovalbumin (ova; a moiety of interest) and the N-terminal ATP binding domain of hsp70 or the C-terminal peptide binding domain of hsp70). Claims 3, 4, 28, 29, 33, 34, 41, and 42 have been amended to provide proper antecedent basis. No new matter has been added.

35 U.S.C. § 112 ¶ 2

The Examiner rejected claims 31 and 44 as being indefinite (Office Action at page 3). As claims 31 and 44 have been canceled, this ground for rejection is now moot.

35 U.S.C. § 112 ¶ 1

The Examiner rejected claims 1-6, 8, 27-35, 37 and 40-44 “as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention” (Office action at page 3). The Examiner emphasizes: **This is a New Matter rejection** (Office action at page 3). More specifically, the Examiner reproduces two phrases that appear in claim 1 (the first is, “a protein consisting of a portion of a (*sic.*) heat shock protein (hsp)” and the second is, “the portion of the hsp is sufficient to deliver the moiety into the cells”) and one phrase that appears in claims 8 and 37 (“protein or peptide is glycosylated”). The Examiner then states that these phrases “represent a departure from the specification and claims

as originally filed and applicant has not pointed out where the support comes (*sic.*) from" (Office action at page 3).

This ground for rejection is traversed in part and is now moot, in part. Claim 1 has been amended to refer to two specific portions of hsp70: the amino terminal ATP binding domain and the carboxyl terminal peptide binding domain, either of which can be covalently linked to the moiety of interest. These portions are disclosed in the original specification. As noted above, Applicant teaches that the hsp can be hsp70 (specification at page 7, line 33) and, in the Examples, Applicant teaches purification of fusion proteins containing ovalbumin (ova; a moiety of interest) and the ATP binding domain of hsp70 or the peptide binding domain of hsp70 (page 28, lines 13-20). Thus, the specification discloses the very portions of hsp70 now recited in claim 1. Accordingly, claim 1 contains no new matter (nor did it prior to the present amendment). As the terms the Examiner relied on are no longer used in claim 1, this ground for rejection is moot.

The phrase, "wherein the protein or peptide is glycosylated," which appears in claims 8 and 37, is fully supported by the specification. The Examiner's attention is directed to the specification at page 5, lines 12-16, where Applicant states that "glycoproteins" can be "delivered into mammalian cells by the present method". It is well known in the art that glycoproteins are glycosylated proteins. *See also* page 8, lines 4-5, and original claims 4, 8, 12, 16, 20, and 24. There is no new matter in claim 8 or claim 37. This ground for rejection should therefore be withdrawn.

35 U.S.C. § 103

The Examiner rejected claims 1-6, 8, 27-35, 37 and 40-44 under 35 U.S.C. § 103(a) as being obvious over Suzue *et al.* (*J. Immunol.*, 1996; herein "Suzue") or over Barrios *et al.* (*Eur. J. Immunol.*, 1992; herein "Barrios") both in view of Srivastava *et al.* (*Curr. Opin. Immunol.*, 1994; herein "Srivastava") and U.S. Patent No. 6,403,099 (herein "Rappuoli"). The Examiner points to Suzue's disclosure of a fusion protein containing mycobacterial hsp70 and the p24 antigen of HIV (Office action at page 4) and to Barrios' disclosure of complexes containing mycobacterial hsp70 and "proteins" (Barrios conjugated the hsp to a synthetic malaria

polypeptide). Turning to the secondary references, the Examiner relies on (1) Srivastava as a teaching that complexes containing an hsp and an antigen are immunogenic and that their immunogenicity is “a function of the uptake of the complex by antigen presenting cells” (Office action at page 5) and (2) Rappuoli as a teaching that a portion of an hsp can be covalently linked to a moiety of interest (Office action at page 5). The Examiner concludes (Office action at page 5):

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of U.S. Patent '099 [Rappuoli] to those of Suzue et al., or Barrios et al to obtain a claimed method of delivering a moiety of interest into a cell, the method comprising contacting the cell with a complex comprising the moiety of interest covalently linked to a portion of a heat shock protein.

As claims 2, 31, 32, and 44 have been canceled and claims 6 and 35 are withdrawn, the rejection is moot with respect to those claims. In view of the present amendment of claim 1, from which the remaining rejected claims (claims 3-5, 8, 27-30, 33-34, 37 and 40-43) depend, this ground for rejection should be withdrawn.

For a *prima facie* case of obviousness, there must be (1) some suggestion or motivation to modify the reference or to combine reference teachings; (2) a reasonable expectation of success; and (3) a teaching or suggestion of all the limitations of the claim. MPEP at 2143. None of these criteria are met in connection with amended claim 1, which now recites particular portions of hsp70: the amino terminal ATP binding domain and the carboxyl terminal peptide binding domain.

More specifically, neither Suzue, Barrios, nor Srivastava suggest that one should form any entity (be that a conjugate or fusion protein) with a portion of an hsp, let alone the portions now claimed, and Rappuoli's disclosure of “domains” or “epitopes” fails as well. Rappuoli states that “the skilled man can readily ascertain for a given heat shock protein which domains or epitopes are responsible for the immunostimulatory action and prepare modified heat shock protein containing only those domains or a sub set thereof” (col. 3, lines 21-25). But Rappuoli does not disclose any such domains for hsp70, nor provide guidance that would lead one to the amino terminal ATP binding domain of an hsp70 or the carboxyl terminal peptide binding

domain of an hsp70, as Applicant now claims. Moreover, there is no motivation in the prior art to modify the full-length hsps used by Suzue, Barrios, and Srivastava, and there is nothing to suggest that one should limit the vaguely described "domains or sub sets (*sic.*) thereof" generally referred to by Rippouli. The prior art must motivate one to make the composition claimed. In the present case, there is simply no teaching of the specific hsp portions Applicant now recited in the claims, nor is there any motivation to modify the hsps previously disclosed to generate those portions. Accordingly, this ground for rejection should be withdrawn.

Change of Correspondence Address

A Change of Correspondence Address is being filed concurrently herewith.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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